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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,804	01/07/2005	Christophe Bonny	25486-501B-NATL	5087

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EXAMINER	
STANDLEY, STEVEN H	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
11/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,804	BONNY, CHRISTOPHE	
	Examiner	Art Unit	
	Steven H. Standley	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I (in part, as it relates to SEQ ID NO: 1-2; 2 being generic to 1) in the reply filed on 10/01/07 is acknowledged. Applicant has cancelled claims 1-24, and submitted new claims 31-36. Claims 25-36 are readable upon the elected invention.

The requirement is still deemed proper and is therefore made FINAL.

On page 5 of Remarks dated 10/01/07, applicant correctly indicates the second paragraph encompasses II-XXXIII, not XXII.

Priority

2. Priority is to provisional application 60/347,062 filed 1/09/02.

Claim Objections

3. Claim 25 is objected to because of the following informalities: It contains reference to 'MKK7,' without first disclosing the meaning of the acronym. In order to make the description of the invention more clear, the first claim that mentions these acronyms should fully express the phrase, and be followed by parentheses, which identify the acronym to be used in the following claim(s). Amendment of claim 25 to include 'MKK7' in parentheses right after the term' Mitogen-activated protein kinase kinase,' would overcome the rejection. Appropriate correction is required.

4. Claim 25, 28, and 30 are objected to because of the following informalities: because it recites, "...and its capable of inhibiting of the binding MKK7..." which is very likely a grammatical error. If the claims were to read, "and **is** capable of inhibiting the binding **of**..." it would obviate the rejection. Appropriate correction is required.

5. Claims 31, 34, and 36 are objected to because of the following informalities: because it recites, "wherein said chimeric peptide and is capable of inhibiting of the binding MKK7..." which is very likely a grammatical error. If the claims were to read, ""wherein said chimeric peptide is capable of inhibiting the binding MKK7..." it would obviate the rejection. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 25-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting apoptosis in a cell in vitro, does not reasonably provide enablement for alleviating a symptom of apoptosis-associated disorder, or for a method of inhibiting apoptosis in vivo or a method of promoting regeneration of neurons or a method of inhibiting apoptosis wherein the disorder is a neurological disorder or neurodegenerative disorder or pancreatic disorder. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The invention is complex because it uses a peptide that binds to a plethora of protein targets with reasonably the same affinity, and yet it must displace MKK7 from insulin binding protein 1 to inhibit apoptosis. This makes it complex because the peptide, an SH3 binding peptide, can effect hundreds of molecules in related and unrelated pathways, yielding complex and for the most part, unexplored consequences. Also, the method is meant to treat apoptosis-related diseases which reasonably include an enormous number of diseases with unrelated symptoms, etiologies, signal transduction pathways, cell types, and mammalian species.

The prior art indicates SH3 domains and the proteins that bind them dos so in an extremely promiscuous fashion. See Mayer (2001) page 1256, right col, wherein he indicates the lack of specificity of SH3 domains indicates they bind multiple, probably even hundreds of targets in a cell. See Rickles et al., wherein they describe the relative

affinities of SH3 domains to a panoply of targets (see table 1, page 10913). Note that the affinities are all within about 100 fold of eachother. Thus, while the applicant has provided in vitro data with homogenous cell types, the art suggests administration to an animal, which is composed of reasonably thousands of cell types would be complicated by the incredibly rich source of targets the instant peptide would potentially bind to and effect. Notwithstanding the extreme promiscuity of these domains, the art is completely silent as to their use as therapeutics. The examiner can find not one molecule designed to specifically effect the interaction between an SH3 domain and its binding protein. Moreover, there has been no validation of any kind in animal models of diseases related to apoptosis, nor any disease for that matter.

The art also suggests that diseases associated with apoptosis are not treated effectively with apoptosis inhibitors. See Waldmeier et al (2006). Thus, it is unpredictable whether the instant peptide would treat any disease.

There are no working examples or guidance wherein the claimed peptide is used to treat anything in vivo. This is particularly important given the known promiscuity of the target and binding proteins. Applicant is using a homogenous population of cells, which does not accurately reflect the enormous number of potential binding partners to the claimed peptide in vivo. Thus, one cannot surmise what the peptide does from in vitro data.

The breadth of the claims are such that they encompass an enormous number of diseases with or without apoptosis as the direct contributing factor. In fact, it is difficult for the examiner to find a disease that is not associated with some apoptosis.

Thus, given the lack of support in the art, the unpredictability of treating an apoptotic disease, the breadth of the claims, and the lack of any in vivo teachings or examples, one of skill in the art could not use this invention commensurate with the scope of the claims.

7. Claims 25-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims a 50 mer containing a designated 12 mer wherein 8 of those amino acids are specified. The 12 mer alone generates 160,000 variants. An additional 38 unspecified amino acids represents a very large number of molecules with little structure and no functional limitations. The claims recite, "..***capable of*** binding..." The examiner notes that "capable of binding" does not require that the variant bind. It only requires it has the potential to bind MKK7. Therefore there is no real functional limitation to the peptides claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed

above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers* v. *Revel*, 25 USPQ2d 1601 at 1606 (CMC 1993) and *Amgen Inc.* v. *Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven Standley whose telephone number is **(571) 272-3432**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on **(571) 272-0867**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Steve Standley, Ph.D.
11/07/07

/DAVID ROMEO/
PRIMARY EXAMINER
ART UNIT 1647